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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/070,329 | 03/05/2002 | Tomomi Ikemoto | 2645 USOP | 7134 |

23115 7590 09/14/2004

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EXAMINER

TUCKER, ZACHARY C

| ART UNIT | PAPER NUMBER |
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1624

DATE MAILED: 09/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/070,329 | Applicant(s) IKEMOTO ET AL. | |
| | Examiner Zachary C. Tucker | Art Unit 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10-12 and 14-30 is/are pending in the application.
- 4a) Of the above claim(s) 1-7 and 16-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 8, 10-12, 14 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Response to Amendment

As requested in the correspondence filed 27 July 2004, which is in reply to the Office action mailed 28 April 2004, claims 9 and 13 have been cancelled, and claims 8 and 12 have been amended. The specification has also been amended at pages 1, 22, 43, 55 and 62 as requested in the correspondence filed 27 July 2004.

Status of Claim Rejections - 35 USC § 112

In the previous Office action, mailed 28 April 2004, claims 8, 10, 11, 12, 14 and 15 were rejected under the first paragraph of 35 U.S.C. 112, for lack of enablement.

In view of the amendment to claims 8 and 12, the rejection is hereby withdrawn.

Although "optionally substituted acyl group" remains indefinite, the amendment to "Y" in claims 8 and 12 sufficiently narrows the scope that group (in claims 8 and 12) so as to be commensurate with the synthetic procedure that the specification teaches for making compounds of the invention.

In the previous Office action, mailed 28 April 2004, claims 8-15 were rejected under the second paragraph of 35 U.S.C. 112 paragraph for indefiniteness of the terms, "heterocyclic" and "optionally substituted."

Claims 9 and 13 have been cancelled, mooted the rejection of those claims under 35 U.S.C., second paragraph.

The rejection of claims 8, 10-12, 14 and 15 under 35 U.S.C. 112, second paragraph, is maintained. Applicant has pointed to the definitions for the objected-to claim language in the specification (which were noted by the examiner in the rejection),

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and alleges that said definitions provide ample definition under 35 U.S.C. 112, second paragraph, for the various 'optionally substituted' identities of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 and R^7 , and for 'heterocyclic.' Although the specification provides some examples of what optional substituents and heterocycles are contemplated by the claim language, no distinct group is pointed out. "May include" prefaces every one of the definitions in the specification. Therefore, one of ordinary skill would no doubt understand some of the scope of what is claimed, but could not possibly be apprised of where lies the delineation between what compounds applicants consider to be within the scope of the claims and what ^{are} ~~is~~ without. Is a tetrachloroethylene group an optional substituent? Is a polyalkoxyalkyl moiety an optional substituent? Is guanidyl? Is a thienothiophene ring within the scope of applicants' "heterocyclic?" Is a cyclic carbonate, a lactone or phosphole? If applicants cannot answer these questions, then how is the public to understand the scope of applicants' claims?

Without any limitation on the character or number of substituents it becomes apparent that "optionally substituted" may be considered inclusive of almost any configuration of atoms and thus, the claims under consideration are of indeterminate scope.

In the previous Office action, the examiner provided evidence that there are at least three slightly different definitions for the general term "heterocyclic" in use by those of ordinary skill.

Applicants' arguments address some language from the decision rendered *In re Paulson* (30 F.3d 1475), with which the examiner does not disagree. This decision was

cited in the previous Office action to illustrate the point that should one use the instant specification to interpret what the patentee meant by a word or phrase in the instant claim (which of course is permissible), he would not be fully apprised of what the phrases "optionally substituted" and "heterocyclic" signify because the definitions provided in the specification are vague, offering only some examples of what "optionally substituted" or "heterocyclic" may include. Interpretation of "optionally substituted" and "heterocyclic" which are recited in the instant claims so as to only be limited to the examples provided for these terms in the specification would fly in the face of the decision from *In re Paulson* because to do so would in fact introduce an 'extraneous' limitation into the claims, said 'extraneous' limitation being replacing open-ended definitions with distinct and concise definitions.

At the top of page 20 of the correspondence filed 27 July 2004, applicants' counsel states "To summarize, the claims indicate that the variables can be substituted; and the specification states what the optional substituents are; so there is no impermissible vagueness." The specification, on the contrary, does not state what the substituents are, only what the substituents may include.

As for the argument that because "optionally substituted" was allowed in other cases, it should also be allowed here, the indefiniteness remains. The U.S. Court of Customs and Patent Appeals wrote *In re Giolito* 188 USPQ 645: "We reject appellants' argument that the instant claims are allowable because similar claims have been allowed in a patent. It is immaterial whether similar claims have been allowed to others. See *In re Margaroli*, 50 CCPA 1400, 318 F.2d 348, 138 USPQ 158 (1963); *In re Wright*,

45 CCPA 1005, 256 F.2d 583, 118 USPQ 287 (1958); *In re Launder*, 41 CCPA 887, 212 F.2d 603, 101 USPQ 391 (1954)".

Lastly, another important point of indefiniteness is presented by the fact that a hydroxyl group (-OH) or thiol group (-SH) ceases to be a hydroxyl group or thiol group when substituted replacing the hydrogen atom (which is the only place where a substituent could be present). Applicants insist, however, that when these groups are substituted, they remain "hydroxyl groups" and "thiol" groups, even though the groups formed by such a substitution are no longer "hydroxyl groups" and "thiol" groups. In view of applicants' distortion of the meaning of the terms "substituted hydroxyl" and "substituted thiol" it is clear that in the context of the invention, a named functional group when substituted, retains its identity as the parent functional group, albeit a substituted one, even if the thusly formed functional group is a different functional group.

Applicants define "substituted hydroxy" and "substituted thiol" on page 19 of the specification as being any hydroxy (-OH) or thiol (-SH) substituted with a substituent that "may include an optionally substituted hydrocarbon group." Thus, the formed functional group could be alkoxy, phenoxy, cycloalkyloxy, alkylthio, phenylthio, an ester, a thioester, amide, thioamide, carbamate, thiocarbamate, *et cetera*. These are not hydroxyl or thiol groups, but the specification defines them as such.

The fact that a substituent could be substituted so as to lose its identity as the parent substituent and remain (in applicants' opinion) merely a 'substituted' version of the parent substituent, further confounds an effort to determine the metes and bounds of what is claimed.

Status of Claim Rejections - 35 USC § 102

In the previous Office action, mailed 28 April 2004, claims 8, 10, 11, 12, 14 and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by US 4,243,678 (Krastinat '678).

The amendment filed 27 July 2004 limits "Y" to an "optionally substituted acyl group," which although indefinite, does not on a phenyl group, as disclosed by Krastinat '678 at the position corresponding to applicants' "Y" group.

The rejection of claims 8, 10, 11, 12 and 14 as being anticipated by Krastinat '678 is hereby withdrawn.

In the previous Office action, mailed 28 April 2004, claims 8, 10, 11, 12 and 14 were rejected under 35 U.S.C. 102(b) as being anticipated by CA 1013960 (Lehman).

The group corresponding to "Y" in Lehman's 4-(N-2',6'-dichloroanilino)butyric acid was chlorine. In view of the amendment filed to claims 8 and 12 filed 27 July 2004, the rejection based on Lehman is hereby withdrawn. Although indefinite, "optionally substituted acyl" which replaces "electron withdrawing group" does not read on a chlorine atom.

In the previous Office action, mailed 28 April 2004, claims 8, 10, 11, 12, 14 and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by GB 2 024 813 A (Krastinat et al).

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Krastinat et al discloses several compounds bearing a phenyl ring at the position corresponding to "Y" in the compounds according to the invention. Although indefinite, "optionally substituted acyl" does not read on a phenyl group.

Accordingly, the rejection of claims 8, 10, 11, 12, 14 as being anticipated by Krastinat et al is hereby withdrawn in view of the amendment filed 27 July 2004.

In the previous Office action, mailed 28 April 2004, claims 8, 10, 11, 12, 14 were rejected under 35 U.S.C. 102(b) as being anticipated by

Berry, et al. "Polychloromatic Compounds. Part V. Preparation and Oxidation of Pentachlorophenyl-substituted Tertiary Amines and Reactions of n-Butyl-lithium and other Nucleophiles with various Pentachlorophenyl Derivatives" JOURNAL OF THE CHEMICAL SOCIETY 1285-1294(1969)

Like Lehman's compounds, the position corresponding to "Y" in the compounds disclosed by Berry et al is a chlorine atom.

In view of the amendment to claims 8 and 12, limiting "Y" to an "optionally substituted acyl group," which although indefinite, does not read on a chlorine atom, the rejection of claims 8, 10, 11, 12, 14 as being anticipated by Berry et al is hereby withdrawn.

Status of Claim Rejections - 35 USC § 103

In the previous Office action, mailed 28 April 2004, claims 8, 10, 11, 12, 14 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 237 918 (Englert).

In view of the amendment filed 27 July 2004, the rejections based on Englert are hereby withdrawn. Englert's only electron-withdrawing groups at the position

corresponding to "Y" in compounds according to the instant claims are halogen, so "optionally substituted acyl," although indefinite, overcomes the Englert rejection.

Upon reconsideration of the pending claims, also bearing in mind that a substituted functional group may actually be, by the substitution, transformed into another functional group (see the discussion of 'optionally substituted hydroxyl' and 'optionally substituted thiol' hereinabove), the following new rejections under 35 U.S.C. 102(b) are seen as necessary.

New Claim Rejections - 35 USC § 102

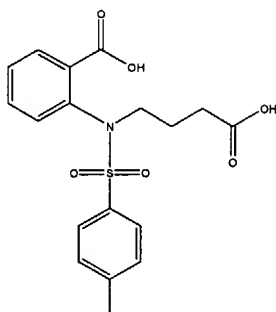
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8, 10, 12 and 14 rejected under 35 U.S.C. 102(b) as being anticipated by Proctor and Thomson, "Azabenzocycloheptenones. Part II. Dieckmann Cyclisation of Arylamino-esters" Journal of the Chemical Society, pages 2312-2314 (1957).

Proctor and Thomson disclose a method for making azabenzocycloheptenones. One of the intermediates is the hydrolysis product of ethyl- γ -N-(2-methoxycarbonylphenyl)-N-toluene-*p*-sulphonamidobutyrate, (crystallized from aq. ethanol as needles on page 2314, third full paragraph) which has this structural formula:

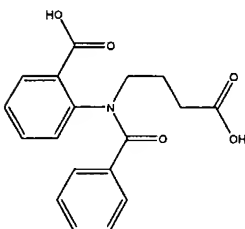


This compound is one according to instant claims 8, 10, 12 and 14 wherein R¹ is a substituted sulphonyl group, R⁶ and R⁷ are joined to form a phenyl ring, R², R³, R⁴ and R⁵ are hydrogen. Group "Y" is a substituted formyl group wherein the substituent is hydroxy. The compound disclosed by Proctor and Thomson reads on compounds according to 8, 10, 12 and 14 because a -C(O)-H (formyl group), when substituted with hydroxy, becomes a substituted version of an acyl group according to the preferred definition.

Claims 8, 10-12, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Brauholtz and Mann, "The Structure and Properties of Certain Polycyclic Indolo- and Quinolono-derivatives. Part XI. Derivatives of 4:5:6:7-Tetrahydro-1-methyl-4-oxo-2:3-benzazepine" Journal of the Chemical Society, pages 3377-3386 (1958).

Brauholtz and Mann teach syntheses of various polycyclic Indolo- and Quinolono-compounds. The reference is interesting for its disclosure of an intermediate which is a compound according to instant claims 8, 10-12, 14 and 15 on page 3383, second paragraph up from the bottom of the page. Hydrolysis of methyl N-benzoyl-N-(3-ethoxycarbonylpropyl)anthranilate in 50% aq. ethanol and sodium hydroxide is reported.

The hydrolysis yields N-benzoyl-N-(3-carboxypropyl)anthranilic acid, which has this structure:

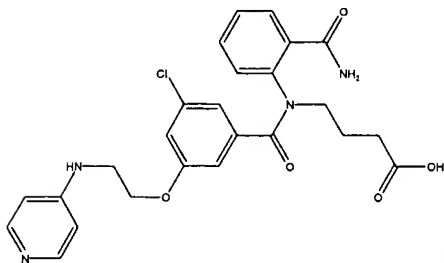


This compound is one according to instant claims 8, 10-12, 14 and 15 wherein wherein R^1 is a substituted hydrocarbon group, wherein the substituents are – oxo and phenyl, R^6 and R^7 are joined to form a phenyl ring, R^2 , R^3 , R^4 and R^5 are hydrogen, and “Y” is a substituted formyl group, wherein the substituent is hydroxy.

Claims 8, 10-12, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/22589 (Watson et al).

Watson et al discloses some thrombin inhibiting pharmaceuticals, one of which is the compound 4-((2-carbamoyl-phenyl)-{3-chloro-5-[2-(pyridin-4-ylamino)-ethoxy]-benzoyl}-amino)-butyric acid (Example 39, page 81).

The compound has this structure:



Watson et al's Example 39 reads on instant claims 8, 10-12, 14 and 15 wherein R^1 is a substituted hydrocarbon group, wherein the substituents are oxo and 3-chloro-[5-(2-pyridin-4-ylamino)]-ethoxyphenyl. R^6 and R^7 are joined to

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form a phenyl ring, R^2 , R^3 , R^4 and R^5 are hydrogen, and "Y" is a substituted formyl group, wherein the substituent is amino.

Conclusion

Due to the new rejections set forth this Office action is non-final.

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday-Friday from 6:30am to 3:00pm. If Attempts to reach the examiner are unsuccessful, the examiner's supervisor, Mukund Shah, can be reached at (571) 272-0674.

If, after a 24-hour period, Dr. Shah is unreachable, contact the examiner's acting supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (703) 308-4556 for regular communications and (703) 308-4242 for after-final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-2717.

zt



MUKUND J. SHAH
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